

**What is Claimed:**

1. A skin permeation enhancer composition for enhancing absorption of a steroid hormone through the skin, wherein the composition comprises a combination of a pharmaceutically acceptable organic solvent, a fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of a hydroxy acid, a lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of a hydroxyl acid, and a C<sub>6</sub>-C<sub>18</sub> fatty acid.
2. The composition of claim 1, wherein the pharmaceutically acceptable organic solvent is dimethyl sulfoxide.
3. The composition of claim 1, wherein the fatty alcohol ester of a hydroxy acid is a fatty alcohol ester of lactic acid.
4. The composition of claim 1, wherein the lower alkyl ester of a hydroxy acid is a lower alkyl ester of lactic acid.
5. The composition of claim 1, wherein the C<sub>6</sub>-C<sub>18</sub> fatty acid is capric acid.
6. The composition of claim 1, comprising dimethyl sulfoxide, a fatty alcohol ester of lactic acid, a lower alkyl ester of lactic acid, and capric acid.
7. The composition of claim 6, wherein the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 2 : 1 : 1 : 0.8 to 6 : 1 : 1 : 0.8, respectively
8. The composition of claim 7, wherein the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 3 : 1 : 1 : 0.8 to 4 : 1 : 1 : 0.8, respectively.
9. The composition of claim 6, wherein the fatty alcohol ester of lactic acid is lauryl lactate.
10. The composition of claim 6, wherein the lower alkyl ester of lactic acid is ethyl lactate.
11. The composition of claim 1, comprising one or more of a progestin, an estrogen and a testosterone hormone.

12. The composition of claim 11, wherein the progestin is levonorgestrel.
13. The composition of claim 11, wherein the estrogen is ethinyl estradiol or 17- $\beta$  estradiol.
14. The composition of claim 1, comprising a progestin and an estrogen in a weight ratio of at least about 1.8 : 1.
15. The composition of claim 14, comprising a progestin and an estrogen in a weight ratio of at least about 2:1.
16. The composition of claim 1, comprising an estrogen in an amount less than about 1.5 percent by weight of the composition.
17. The composition of claim 1, comprising a testosterone.
18. The composition of claim 1, comprising a progestin, an estrogen and a testosterone.
19. The composition of claim 1, comprising dimethyl sulfoxide, lauryl lactate, ethyl lactate and capric acid in a weight ratio of about 3 : 1 : 1 : 0.8.
20. The composition of claim 19, comprising levonorgestrel and ethinyl estradiol in a weight ratio of about 1.8 : 1, wherein the ethinyl estradiol comprises less than about 1.5% by weight of the composition.
21. A polymer formulation for use in fabricating a transdermal hormone delivery system of a type comprising a backing layer and a polymer matrix in which is dispersed one or more steroid hormones to be transdermally delivered, wherein the formulation comprises a polymer and, on a weight percentage basis, from about 0% to about 5% humectant/plasticizer, and from about 10% to about 30% of a skin permeation enhancer composition comprising a combination of a pharmaceutically acceptable organic solvent, a fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of a hydroxy acid, a lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of a hydroxy acid, and a C<sub>6</sub>-C<sub>18</sub> fatty acid.
22. The formulation of claim 21, wherein the polymer is an adhesive polymer.
23. The formulation of claim 22, wherein the adhesive polymer is a polyacrylate adhesive copolymer.

24. The formulation of claim 23, wherein the polyacrylate adhesive copolymer comprises a 2-ethylhexyl acrylate monomer.
25. The formulation of claim 24, wherein the polyacrylate adhesive copolymer further comprises about 3% to about 60% w/w vinyl acetate.
26. The formulation of claim 21, wherein the humectant/plasticizer is a polyvinylpyrrolidone/vinyl acetate.
27. The formulation of claim 21, wherein the pharmaceutically acceptable organic solvent is dimethyl sulfoxide.
28. The formulation of claim 21, wherein the fatty alcohol ester of a hydroxy acid is a fatty alcohol ester of lactic acid.
29. The formulation of claim 21, wherein the lower alkyl ester of a hydroxy acid is a lower alkyl ester of lactic acid.
30. The formulation of claim 21, wherein the C<sub>6</sub>-C<sub>18</sub> fatty acid is capric acid.
31. The formulation of claim 21, comprising dimethyl sulfoxide, a fatty alcohol ester of lactic acid, a lower alkyl ester of lactic acid, and capric acid.
32. The formulation of claim 31, wherein, prior to drying, the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 2 : 1 : 1 : 0.8 to 6 : 1 : 1 : 0.8, respectively.
33. The formulation of claim 32, wherein the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 3 : 1 : 1 : 0.8 to 4 : 1 : 1 : 0.8, respectively.
34. The formulation of claim 32 which, upon coating upon a backing layer and drying under conditions suitable to form an adhesive polymer matrix for delivering steroid hormones, comprises the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid in a weight ratio of about 4-8 parts dimethyl sulfoxide, about 4-8 parts fatty

alcohol ester of lactic acid, about 1 part lower alkyl ester of lactic acid and about 3-6 parts capric acid.

35. The formulation of claim 34, wherein after the drying the dimethyl sulfoxide and the fatty alcohol ester of lactic acid are present in a weight ratio of between about 1.5 : 1 and about 1 : 1.5.

36. The formulation of claim 34, wherein the drying conditions are about 15 minutes at about 60°C.

37. The formulation of claim 31, wherein the fatty alcohol ester of lactic acid is lauryl lactate.

38. The formulation of claim 31, wherein the lower alkyl ester of lactic acid is ethyl lactate.

39. The formulation of claim 21, comprising a progestin.

40. The formulation of claim 39, wherein the progestin is levonorgestrel.

41. The formulation of claim 21, comprising a progestin and an estrogen.

42. The formulation of claim 41, wherein the progestin and the estrogen are present in a weight ratio of at least 1.8 : 1.

43. The formulation of claim 42, wherein the progestin and the estrogen are present in a weight ratio of at least 2 : 1.

44. The formulation of claim 41, wherein the estrogen comprises less than about 0.3% on a weight basis of the formulation.

45. The formulation of claim 41, wherein the progestin is levonorgestrel and the estrogen is ethynodiol diacetate or 17 $\beta$ -estradiol.

46. The formulation of claim 45, comprising, on a weight percentage basis, about 79.65% polyacrylate adhesive copolymer, about 1.25% polyvinylpyrrolidone/vinyl acetate, about 9.51% dimethyl sulfoxide, about 3.10% lauryl lactate, about 3.10% ethyl lactate, about 2.39% capric acid, about 0.58% levonorgestrel and about 0.28% ethynodiol diacetate.

47. The formulation of claim 46 which, upon coating upon a backing layer and drying under conditions suitable to form an adhesive polymer matrix for delivering steroid hormones, comprises, on a weight percentage basis of the adhesive polymer matrix, from about 4% to about 12% dimethyl sulfoxide, from about 4.2% to about 12.6% lauryl lactate, from about 0.7% to about 2.3% ethyl lactate, and from about 3% to about 9% capric acid.
48. The formulation of claim 47, wherein the drying conditions are about 15 minutes at about 60°C.
49. The formulation of claim 41, which further comprises a testosterone.
50. The formulation of claim 21, comprising a testosterone.
51. A transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and one or more steroid hormones to be delivered transdermally, and an adhesive polymer matrix affixed to the backing layer, wherein the adhesive polymer matrix comprises an adhesive polymer and further comprises, on a final weight percentage basis of the adhesive polymer matrix:
  - a) from about 0% to about 5% of a humectant/plasticizer;
  - b) from about 12% to about 36% percent of a combination of skin permeation enhancing agents which is a mixture comprising from about 4% to about 12% pharmaceutically acceptable organic solvent, from about 4.2% to about 12.6% fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of a hydroxy acid, from about 0.7% to about 2.3% lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of a hydroxy acid, and from about 3% to about 9% C<sub>6</sub>-C<sub>18</sub> fatty acid; and
  - c) an amount of one or more steroid hormones effective to provide a pre-determined daily dose of the one or more hormones for between about one and about nine days.
52. The transdermal hormone delivery system of claim 51, comprising a progestin and an estrogen.
53. The transdermal hormone delivery system of claim 52, further comprising a testosterone.
54. The transdermal hormone delivery system of claim 51, comprising only a progestin.
55. The transdermal hormone delivery system of claim 51, comprising only a testosterone.

56. The transdermal hormone delivery system of claim 51, wherein the progestin is levonorgestrel.
57. The transdermal hormone delivery system of claim 51, wherein the estrogen is ethinyl estradiol or 17  $\beta$ -estradiol.
58. The transdermal hormone delivery system of claim 51, wherein the humectant/plasticizer is a polyvinylpyrrolidone/vinyl acetate.
59. The transdermal hormone delivery system of claim 51, wherein the adhesive polymer comprises a polyacrylate copolymer.
60. The transdermal hormone delivery system of claim 59, wherein the polyacrylate copolymer comprises a 2-ethylhexyl acrylate monomer.
61. The transdermal hormone delivery system of claim 60, wherein the polyacrylate copolymer further comprises about 3 to 60% w/w vinyl acetate.
62. The transdermal hormone delivery system of claim 51, wherein the pharmaceutically acceptable organic solvent is dimethyl sulfoxide.
63. The transdermal hormone delivery system of claim 51, wherein the fatty alcohol ester of a hydroxy acid is a fatty alcohol ester of lactic acid.
64. The transdermal hormone delivery system of claim 51, wherein the lower alkyl ester of a hydroxy acid is a lower alkyl ester of lactic acid.
65. The transdermal hormone delivery system of claim 51, wherein the C<sub>6</sub>-C<sub>18</sub> fatty acid is capric acid.
66. The transdermal hormone delivery system of claim 51, comprising dimethyl sulfoxide, a fatty alcohol ester of lactic acid, a lower alkyl ester of lactic acid, and capric acid.
67. The transdermal hormone delivery system of claim 66, wherein the fatty alcohol ester of lactic acid is lauryl lactate.

68. The transdermal hormone delivery system of claim 66, wherein the lower alkyl ester of lactic acid is ethyl lactate.
69. The transdermal hormone delivery system of claim 66, wherein the skin permeation enhancing agents are present in a weight ratio of about 4-8 parts dimethyl sulfoxide, about 4-8 parts fatty alcohol ester of lactic acid, about 1 part lower alkyl ester of lactic acid and about 3-6 parts capric acid.
70. The transdermal hormone delivery system of claim 66, wherein the dimethyl sulfoxide and the fatty alcohol ester of lactic acid are present in a weight ratio of between about 1.5 : 1 and about 1 : 1.5.
71. The transdermal hormone delivery system of claim 52, formulated for delivery of ethinyl estradiol and levonorgestrel, wherein the ethinyl estradiol is transdermally delivered at a rate of between about 10  $\mu$ g and 50  $\mu$ g per day for a term of about one day to about nine days, and the levonorgestrel is transdermally delivered at a rate of at least 20  $\mu$ g per day for a term of about one day to about nine days.
72. The transdermal hormone delivery system of claim 71, wherein the levonorgestrel is transdermally delivered at a rate of at least 30  $\mu$ g per day for a term of about one day to about nine days.
73. The transdermal hormone delivery system of claim 71, wherein the levonorgestrel is transdermally delivered in an amount sufficient to produce a steady state serum concentration of at least 1,000 pg/ml.
74. The transdermal hormone delivery system of claim 51, wherein the adhesive polymer matrix has a thickness of about 10 to about 300  $\mu$ m.
75. The transdermal hormone delivery system of claim 51, wherein the adhesive polymer matrix has a surface area of about 20  $\text{cm}^2$  or less.
76. The transdermal hormone delivery system of claim 75, wherein the adhesive polymer matrix has a surface area of about 17.5  $\text{cm}^2$  or less.

77. The transdermal hormone delivery system of claim 51, which further comprises an overlay layer, wherein the overlay layer is coated with an adhesive and extends beyond the perimeter of part or all of the backing layer and adhesive polymer matrix.

78. The transdermal hormone delivery system of claim 77, wherein the overlay layer is fabricated with the system, so as to be affixed to the non-dermal side of the backing layer.

79. The transdermal hormone delivery system of claim 77, wherein the overlay layer is fabricated separately from the system.

80. The transdermal hormone delivery system of claim 77, wherein a non-adhesive polymer is substituted for the adhesive polymer, and wherein skin adhesion is effected through the adhesive-coated overlay layer.

81. A method of making a transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and an adhesive polymer matrix comprising one or more steroid hormones to be delivered transdermally, comprising the steps of:

a) formulating an adhesive polymer starting solution by combining an adhesive polymer with, on a weight percentage basis of the adhesive polymer starting solution:

1) from about 0% to about 5% of a humectant/plasticizer;  
2) from about 10% to about 30% percent of a combination of skin permeation enhancing agents which is a mixture comprising a pharmaceutically acceptable organic solvent, a fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of a hydroxy acid, a lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of a hydroxy acid, and a C<sub>6</sub>-C<sub>18</sub> fatty acid; and

3) an amount of one or more of the steroid hormones effective to provide a pre-determined daily dose of the hormone for between about one and about nine days, thereby forming an adhesive polymer starting solution;

b) coating the adhesive polymer starting solution onto the backing layer; and

c) drying the coated backing layer for a time and at a temperature sufficient to produce a transdermal hormone delivery system wherein the adhesive polymer matrix is less than 300 μm thick and wherein the skin permeation enhancing agents are present in amounts of from about 4% to about 12% pharmaceutically acceptable organic solvent, from about 4.2% to about 12.6% fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of hydroxy acid, from about 0.7% to about 2.3% lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of hydroxy acid, and from about 3% to about 9% C<sub>6</sub>-C<sub>18</sub> fatty acid.

82. The method of claim 81, wherein the adhesive polymer starting solution is coated onto the backing layer at a thickness of between about 300  $\mu\text{m}$  and about 800  $\mu\text{m}$ .
83. The method of claim 81, wherein the coated backing layer is dried for between about 5 minutes and about 25 minutes.
84. The method of claim 81, wherein the coated backing layer is dried at a temperature between about 40°C and about 80°C.
85. The method of claim 81, wherein, following drying, the transdermal hormone delivery system is provided with a releasable liner affixed to the adhesive polymer matrix.
86. The method of claim 85, wherein, following drying, the transdermal hormone delivery system is provided with an overlay layer, wherein the overlay layer is coated with an adhesive and extends beyond part or all of the perimeter of the backing layer and adhesive polymer matrix.
87. The method of claim 86, wherein the overlay layer is fabricated separately from the transdermal hormone delivery system and provided with its own releasable liner.
88. The method of claim 86, wherein the overlay layer is fabricated together with the transdermal hormone delivery system, and the system with overlay provided with the releasable liner affixed to the adhesive of the overlay layer and the adhesive polymer matrix.
89. The method of claim 81, wherein the adhesive polymer starting solution is coated onto the backing layer at a thickness of between about 600  $\mu\text{m}$  and 700  $\mu\text{m}$ , and the coated backing layer is dried for between about 13 and 17 minutes at about 55°C - 65°C.
90. A method of administering to a subject one or more of a progestin, estrogen or testosterone hormone, the method comprising applying to the skin of the subject desiring such treatment the one or more hormones dispersed within a skin permeation enhancer composition comprising a combination of a pharmaceutically acceptable organic solvent, a fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of a hydroxy acid, a lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of a hydroxy acid, and a C<sub>6</sub>-C<sub>18</sub> fatty acid.

91. The method of claim 90, wherein the pharmaceutically acceptable organic solvent is dimethyl sulfoxide.
92. The method of claim 90, wherein the fatty alcohol ester of a hydroxy acid is a fatty alcohol ester of lactic acid.
93. The method of claim 90, wherein the lower alkyl ester of a hydroxy acid is a lower alkyl ester of lactic acid.
94. The method of claim 90, wherein the C<sub>6</sub>-C<sub>18</sub> fatty acid is capric acid.
95. The method of claim 90, comprising dimethyl sulfoxide, a fatty alcohol ester of lactic acid, a lower alkyl ester of lactic acid, and capric acid.
96. The method of claim 95, wherein the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 2 : 1 : 1 : 0.8 to 6 : 1 : 1 : 0.8, respectively
97. The method of claim 96, wherein the dimethyl sulfoxide, fatty alcohol ester of lactic acid, lower alkyl ester of lactic acid, and capric acid, are present in a weight ratio of 3 : 1 : 1 : 0.8 to 4 : 1 : 1 : 0.8, respectively.
98. The method of claim 95, wherein the fatty alcohol ester of lactic acid is lauryl lactate.
99. The method of claim 96, wherein the lower alkyl ester of lactic acid is ethyl lactate.
100. A method of administering to a subject one or more of a progestin, estrogen or testosterone hormone, the method comprising applying to the skin of a subject desiring such treatment a transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and the one or more hormones to be delivered transdermally, and an adhesive polymer matrix affixed to the backing layer, wherein the adhesive polymer matrix comprises an adhesive copolymer and further comprises, on a final weight percentage basis of the adhesive polymer matrix:
  - a) from about 0% to about 5% of a humectant/plasticizer;
  - b) from about 12% to about 36% percent of a combination of skin permeation enhancing

agents which is a mixture comprising from about 4% to about 12% pharmaceutically acceptable organic solvent, from about 4.2% to about 12.6% fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of hydroxy acid, from about 0.7% to about 2.3% lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of hydroxy acid, and from about 3% to about 9% C<sub>6</sub>-C<sub>18</sub> fatty acid; and

c) an amount of the one or more progestin, estrogen or testosterone hormones, sufficient to provide an effective dose of the hormone.

101. The method of claim 100, wherein the effective dose is delivered for a period comprising a pre-determined number of days.

102. The method of claim 101, wherein the transdermal hormone delivery system is replaced once each period for successive periods extending as treatment is desired.

103. The method of claim 100, wherein the transdermal hormone delivery system delivers levonorgestrel.

104. The method of claim 100, wherein the transdermal hormone delivery system delivers ethinyl estradiol or 17  $\beta$ -estradiol.

105. The method of claim 102, adapted for control of fertility, wherein the transdermal hormone delivery system provides a pre-determined fertility-controlling daily dose of a progestin and an estrogen for between about 1 and about 9 days, and the transdermal hormone delivery system is replaced once each week for three of four successive weeks of a menstrual cycle, for successive menstrual cycles extending as fertility control is desired.

106. The method of claim 105, wherein the transdermal hormone delivery system is formulated for delivery of ethinyl estradiol and levonorgestrel, wherein the ethinyl estradiol is transdermally delivered at a rate of between about 10  $\mu$ g and 50  $\mu$ g per day for a term of about one day to about one week, and the levonorgestrel is transdermally delivered at a rate of at least 20  $\mu$ g per day for a term of about one day to about nine days.

107. The method of claim 106, wherein the levonorgestrel is transdermally delivered at a rate of at least 30  $\mu$ g per day for a term of about one day to about nine days.

108. The method of claim 105, wherein the levonorgestrel is transdermally delivered in an amount sufficient to produce a steady state serum concentration of at least 1,000 pg/ml and the ethinyl estradiol is transdermally delivered in an amount sufficient to produce a serum concentration of between about 20 and about 80 pg/ml.

109. The method of claim 100, wherein the transdermal hormone delivery system is formulated for delivery of a progestin alone.

110. The method of claim 105, adapted for substantially eliminating menses, wherein the transdermal hormone delivery system is replaced once each week for a desired number of successive weeks, extending as fertility control and elimination of menses are desired.

111. A method of improving libido comprising applying to the skin of a subject desiring such treatment a transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and testosterone hormones to be delivered transdermally, and an adhesive polymer matrix affixed to the backing layer, wherein the adhesive polymer matrix comprises an adhesive copolymer and further comprises, on a final weight percentage basis of the adhesive polymer matrix:

- a) from about 0% to about 5% of a humectant/plasticizer;
- b) from about 12% to about 36% percent of a combination of skin permeation enhancing agents which is a mixture comprising from about 4% to about 12% pharmaceutically acceptable organic solvent, from about 4.2% to about 12.6% fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of hydroxy acid, from about 0.7% to about 2.3% lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of hydroxy acid, and from about 3% to about 9% C<sub>6</sub>-C<sub>18</sub> fatty acid; and
- c) an amount of a testosterone hormone, sufficient to provide an effective dose of the hormone.

112. The method of claim 111, wherein the effective dose is delivered for a period comprising a pre-determined number of days.

113. The method of claim 112, wherein the transdermal hormone delivery system is replaced once each period for successive periods extending as treatment is desired.

114. A transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and one or more hormones to be delivered

transdermally, and an adhesive polymer matrix affixed to the backing layer and comprising a pre-determined amount of the hormones, wherein the adhesive polymer matrix has a surface area of about 20 cm<sup>2</sup> or less and a thickness of about 300 µm or less and the delivery system is capable of delivering at least 20 µg/day levonorgestrel for between about one and about nine days.

115. The transdermal hormone delivery system of claim 114, capable of delivering at least 30 µg/day levonorgestrel for between about one and about nine days.

116. The transdermal hormone delivery system of claim 114, which further comprises an overlay layer, wherein the overlay layer is coated with an adhesive and extends beyond the perimeter of part or all of the backing layer and adhesive polymer matrix.

117. The transdermal hormone delivery system of claim 116, wherein the overlay layer is fabricated with the system, so as to be affixed to the non-dermal side of the backing layer.

118. The transdermal hormone delivery system of claim 116, wherein the overlay layer is fabricated separately from the system.

119. The transdermal hormone delivery system of claim 116, wherein a non-adhesive polymer is substituted for the adhesive polymer, and wherein skin adhesion is effected through the adhesive-coated overlay layer.

120. The transdermal hormone delivery system of claim 114, formulated for delivery of levonorgestrel.

121. The transdermal hormone delivery system of claim 120, which delivers an amount of levonorgestrel sufficient to impart a steady state serum concentration of levonorgestrel of at least 1,000 pg/ml.

122. The transdermal hormone delivery system of claim 120, formulated for delivery of levonorgestrel and an estrogen selected from the group consisting of ethinyl estradiol and 17  $\beta$ -estradiol.

123. The transdermal hormone delivery system of claim 122, wherein the estrogen is ethinyl estradiol and the ethinyl estradiol is transdermally delivered at between 10 µg and 50 µg per day for between about one and about nine days.

124. The transdermal hormone delivery system of claim 114, formulated for delivery of a progestin alone.

125. The transdermal hormone delivery system of claim 114, formulated for delivery of a progestin, an estrogen and a testosterone.

126. The transdermal hormone delivery system of claim 114, formulated for delivery of a testosterone alone.

127. The transdermal hormone delivery system of claim 114, wherein the adhesive polymer matrix comprises an adhesive polymer and further comprises, on a final weight percentage basis of the adhesive polymer matrix:

a) from about 0% to about 5% of a humectant/plasticizer;

b) from about 12% to about 36% percent of a combination of skin permeation enhancing agents which is a mixture comprising from about 4% to about 12% pharmaceutically acceptable organic solvent, from about 4.2% to about 12.6% fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of hydroxy acid, from about 0.7% to about 2.3% lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of hydroxy acid, and from about 3% to about 9% C<sub>6</sub>-C<sub>18</sub> fatty acid; and

c) an amount of the one or more progestin, estrogen or testosterone hormones, effective to provide a pre-determined daily dose of each hormone for between about one and about nine days.

128. The transdermal hormone delivery system of claim 127, wherein the humectant/plasticizer is a polyvinylpyrrolidone/vinyl acetate.

129. The transdermal hormone delivery system of claim 127, wherein the adhesive polymer comprises a polyacrylate copolymer.

130. The transdermal hormone delivery system of claim 129, wherein the polyacrylate copolymer comprises a 2-ethylhexyl acrylate monomer.

131. The transdermal hormone delivery system of claim 129, wherein the polyacrylate copolymer further comprises about 3 to 60% w/w vinyl acetate.
132. The transdermal hormone delivery system of claim 127, wherein the pharmaceutically acceptable organic solvent is dimethyl sulfoxide.
133. The transdermal hormone delivery system of claim 127, wherein the fatty alcohol ester of a hydroxy acid is a fatty alcohol ester of lactic acid.
134. The transdermal hormone delivery system of claim 127, wherein the lower alkyl ester of a hydroxy acid is a lower alkyl ester of lactic acid.
135. The transdermal hormone delivery system of claim 127, wherein the C<sub>6</sub>-C<sub>18</sub> fatty acid is capric acid.
136. The transdermal hormone delivery system of claim 127, comprising dimethyl sulfoxide, a fatty alcohol ester of lactic acid, a lower alkyl ester of lactic acid, and capric acid.
137. The transdermal hormone delivery system of claim 136, wherein the fatty alcohol ester of lactic acid is lauryl lactate.
138. The transdermal hormone delivery system of claim 136, wherein the lower alkyl ester of lactic acid is ethyl lactate.
139. The transdermal hormone delivery system of claim 136, wherein the skin permeation enhancing agents are present in a weight ratio of about 4-8 parts dimethylsulfoxide, about 4-8 parts fatty alcohol ester of lactic acid, about 1 part lower alkyl ester of lactic acid and about 3-6 parts capric acid.
140. The transdermal hormone delivery system of claim 139, wherein the dimethyl sulfoxide and the fatty alcohol ester of lactic acid are present in a weight ratio of between about 1.5 : 1 and about 1 : 1.5.
141. A method of making a transdermal hormone delivery system comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and an adhesive polymer matrix comprising one or more progestin, estrogen or testosterone hormones to be delivered

transdermally, comprising the steps of:

- a) formulating an adhesive polymer starting solution by combining an adhesive polymer with, on a weight percentage basis of the adhesive polymer starting solution:
  - 1) from about 0% to about 5% of a humectant/plasticizer;
  - 2) from about 10% to about 30% percent of a combination of skin permeation enhancing agents which is a mixture comprising a pharmaceutically acceptable organic solvent, a fatty (C<sub>8</sub>-C<sub>20</sub>) alcohol ester of hydroxy acid, a lower (C<sub>1</sub>-C<sub>4</sub>) alkyl ester of hydroxy acid, and a C<sub>6</sub>-C<sub>18</sub> fatty acid; and
  - 3) an amount of the one or more progestin, estrogen or testosterone hormones effective to provide a pre-determined daily dose of each hormone for a period comprising a pre-determined number of days;
- b) coating the adhesive polymer starting solution onto the backing layer; and
- c) drying the coated backing layer for a time and at a temperature sufficient to produce a transdermal hormone delivery system wherein the adhesive polymer matrix has a surface area of about 20 cm<sup>2</sup> or less and a thickness of about 300 µm or less and the delivery system is capable of delivering at least 20 µg/day levonorgestrel for between about one and about nine days.

142. The method of claim 141, wherein the adhesive polymer matrix starting solution is coated onto the backing layer at a thickness of between about 300 µm and about 800 µm.

143. The method of claim 141, wherein the coated backing layer is dried for between about 5 minutes and about 25 minutes.

144. The method of claim 141, wherein the coated backing layer is dried at a temperature between about 40°C and about 80°C.

145. The method of claim 141, wherein, following drying, the transdermal hormone delivery system is provided with a releasable liner affixed to the adhesive polymer matrix.

146. The method of claim 145, wherein, following drying, the transdermal hormone delivery system is provided with an overlay layer, wherein the overlay layer is coated with an adhesive and extends beyond the perimeter of part or all the backing layer and adhesive polymer matrix.

147. The method of claim 146, wherein the overlay layer is fabricated separately from the transdermal hormone delivery system and provided with its own releasable liner.

148. The method of claim 146, wherein the overlay layer is fabricated together with the transdermal hormone delivery system, and the system with overlay provided with the releasable liner affixed to the adhesive of the overlay layer and the adhesive polymer matrix.

149. The method of claim 141, wherein the adhesive polymer matrix starting solution is coated onto the backing layer at a thickness of between about 600  $\mu\text{m}$  and 700  $\mu\text{m}$ , and the coated backing layer is dried for between about 13 and 17 minutes at about 55°C - 65°C.

150. A method of administering to a subject one or more of a progestin, estrogen or testosterone hormone, the method comprising applying to the skin of a subject desiring such treatment a transdermal hormone delivery comprising a backing layer that is substantially impermeable to skin permeation enhancing agents and the hormones to be delivered transdermally, and an adhesive polymer matrix affixed to the backing layer and comprising the one or more progestin, estrogen or testosterone hormones, wherein the adhesive polymer matrix is of a maximum surface area of about 20  $\text{cm}^2$  and a maximum thickness of about 300  $\mu\text{m}$  and the delivery system is capable of delivering at least 20  $\mu\text{g}/\text{day}$  levonorgestrel for between about one and about nine days.

151. The method of claim 150, wherein the transdermal hormone delivery system is replaced periodically for successive periods extending as treatment is desired.

152. The method of claim 150, wherein the transdermal hormone delivery system delivers levonorgestrel.

153. The method of claim 150, wherein the transdermal hormone delivery system delivers ethinyl estradiol or 17  $\beta$ -estradiol.

154. The method of claim 151, adapted for control of fertility, wherein the transdermal hormone delivery system provides a pre-determined fertility-controlling daily dose of a progestin and an estrogen for between about 1 and about 9 days, and the transdermal hormone delivery system is replaced once each week for three of four successive weeks of a menstrual cycle, for successive menstrual cycles extending as fertility control is desired.

155. The method of claim 154, wherein the transdermal hormone delivery system delivers levonorgestrel.

156. The method of claim 155, wherein the transdermal hormone delivery system delivers ethinyl estradiol or 17  $\beta$ -estradiol.

157. The method of claim 154, wherein the transdermal hormone delivery system is formulated for delivery of ethinyl estradiol and levonorgestrel, wherein the ethinyl estradiol is transdermally delivered at a rate of between about 10  $\mu$ g and 50  $\mu$ g per day for a term of about one day to about one week, and the levonorgestrel is transdermally delivered at a rate of at least 20  $\mu$ g per day for a term of about one day to about nine days.

158. The method of claim 157, wherein the levonorgestrel is transdermally delivered at a rate of at least 30  $\mu$ g per day for a term of about one day to about nine days.

159. The method of claim 157, wherein the levonorgestrel is transdermally delivered in an amount sufficient to produce a steady state serum concentration of at least 1,000 pg/ml and the ethinyl estradiol is transdermally delivered in an amount sufficient to produce a serum concentration of between about 20 and about 80 pg/ml.

160. The method of claim 150, wherein the transdermal hormone delivery system is formulated for delivery of a progestin alone.

161. The method of claim 150, wherein the transdermal hormone delivery system is formulated for delivery of a testosterone in addition to the progestin and the estrogen.

162. The method of claim 154, adapted for substantially eliminating menses, wherein the transdermal hormone delivery system is replaced once each week for a desired number of successive weeks, extending as fertility control and elimination of menses are desired.